HHS FDA CDER

Moderator: Randi Clark
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Coordinator: Welcome and thank you for standing by. All participants will be in listen only mode until the question and answer session. At that time, to request to ask a question, please press star then one. Today's conference is being recorded, if you have any objections, you may disconnect at this time. I would like to turn this meeting over to your host, Sandra Kweder- you may begin.

Sandra Kweder: Good afternoon everyone or good morning, depending on where you're calling from - this is Dr. Sandra Kweder, I'm the Deputy Director of the Office of New Drugs at FDA. I want to thank you for joining us and welcome you to the continued conversation about CFS and ME - we are happy that we have a large number of participants. We can see on the phone line that people continue to join us, so we look forward to a good discussion.

What I'd like to do is, I'd like to - before we begin, I'd like you to hear the voices of people who are here from FDA, unfortunately there are too many other people on the phone to go through the entire list of call participants but so that you get to hear a voice in case you hear it again when someone might be answering a question, I'll ask people around me to introduce themselves now - again, I'm Dr. Sandra Kweder.

Janet Norden: Janet Norden from the Office of Medical Policy in the Center for Drugs.

Mary Gross: Mary Gross Office of Executive Programs in CDER

Janet Maynard: Hi, I'm Janet Maynard with the Division of Pulmonary, Allergy, and Rheumatology Products in the Office of New Drugs.

Sara Eggers: My name is Sara Eggers and I'm with CDER's Office of Strategic Programs.

Randi Clark: I'm Randi Clark, and I'm with CDER's Office of Executive Programs.

Theresa Mullin: (Theresa Mullin) I'm with the Office of Strategic Programs in CDER.

John Whyte: (Dr. John Whyte) from the Safe Use Staff.

Theresa Michele: And Dr. Teresa Michele, in the Division of Pulmonary, Allergy, and Rheumatology Products.

Sandra Kweder: Okay - well thank you everyone, thank you very much folks for speaking up and letting everyone hear your voice.

We thought that probably the best way to proceed today is for us at FDA to share with you what we are doing in follow-up to the workshop that we sponsored last April - April 25 and 26 to be specific as well as to let you know what other fronts we feel like we're making progress on in trying to facilitate drug development for ME/CFS.

To keep you from being completely bored out of your mind, we're going to have a couple of people present. The first speaker will be Sara Eggers who will talk about the workshop and some of the follow-up to that. Sara will be followed by Theresa Michele and Janet Maynard who will talk about some

other activities that we have on-going. And after they're done speaking, then what we'll do is we'll open the phone line up for questions about - I'll try to organize the question-and-answer topics a little bit to specifically follow-up on what they've presented and then we'll move on to other more general questions in a more open dialogue forum.

I do want - someone did suggest that we point out that we are working officially and legally even though the government is partially shut-down. Our operations here related to drug development at FDA are continuing on uninterrupted and we're delighted about that and delighted to be here with you today.

So what I'd like to do now is turn it over to Sara Eggers who will talk a little bit about what's happening in follow-up to the workshop activity - Sara.

Sara Eggers: Thank you Dr. Kweder, and my name is Sara Eggers and you may recognize me if you were at the workshop - I was the facilitator on the first day, the afternoon - and I'm going to first talk about that first afternoon on April 25 and then I'll give a brief overview of April 26.

The April 25 portion of the workshop was conducted as part of FDA's Patient Focus Drug Development initiative and we gave a big background on that initiative as part of the meeting, but I know that that was a while ago and maybe some of you weren't there - so, let me describe a bit about what the Patient Focus Development initiative is - it's a commitment that FDA has made under the authorization of the Prescription Drug User Fee Act - and the intent is to more systematically gather patients' perspectives on specific aspects of their conditions and available therapies to treat their conditions.

Patients have a unique ability to contribute to the understanding of this important context of the disease and this is important to drug development in many ways, including FDA's assessment of the benefits and risks of the drugs that seek marketing approval.

So as part of this commitment, FDA is holding at least 20 public meetings over a five year period, each focused on a specific disease area. And CFS and ME was the first meeting of this kind and it really has served as a great model for our program as a whole. We are very happy with how the meeting has turned out.

It gave us the opportunity to hear directly from patients, care-takers and other patient representatives about your experiences with the debilitating condition. Our discussion that first afternoon focused on two topics, disease symptoms and daily impacts that matter most to patients and current approaches to treating CFS and ME.

For each topic, a panel of patients and patient representatives shared comments to begin a dialogue and this was followed by a facilitated discussion with all patients and patient representatives in the audience. Participants who joined by the web cast were also able to add comments and everyone - patients and others - were encouraged to submit comments on the topic to a public docket. And that is, that anyone could go to a specific page on the regulations.gov Website and send us a statement.

The docket was open from March 11 - when we announced the April meeting - until it was closed on August 2. On September 18, maybe 19 - September 19, I believe - we posted our summary report of that meeting to the Patient-Focus Drug Development website and that information can be found on the link that was in your event invitation.

The report incorporates the input from the in-person and webcast participants as well as the comments submitted to the docket. It's organized around those two main topics - first the symptoms that matter most and the impact they have on daily life and second, the range of treatments currently used to treat CFS and ME.

Our goal was to faithfully recount patients' voices using your own words as much as possible and really reflecting your perspective in a way that is most helpful to FDA.

The input that we got and reported in our report underscores the chronic and debilitating nature of CFS and ME which can severely affect a patient's day-to-day functioning and have a devastating impact on a patient's life and the lives of their families.

The availability and current approach to treatment is striking. Patients' have tried a wide range of drug and non-drug therapies with various effectiveness and for some none are effective.

FDA will carefully consider this input as we fulfill our goal in the drug development process, such as advising sponsors on drug development programs and assessing products under review for marketing approval.

We also believe that this input may have value to drug development more broadly. For example, as drug developers explore potential areas that are needed for CFS and ME patients - or point to the potential need for development qualification of these outcome measures - such as those related to cognitive functioning, in clinical trials.

We have received very positive feedback from our FDA colleagues on the value of this report. We have also received the appreciation and positive and constructive feedback from the patient community. And that's really important to us, we are - we're delighted to hear that many of you felt that the report was thorough and fair in its depiction.

Many of you contributed in some way to our effort - approximately 150 people attended the meeting in person, 300 on the web and 220 comments were submitted to the public docket. The success of this first meeting is really in large part to the tremendous participation and feedback from patients, care givers and advocates who contributed to the meeting.

We have learned a lot from the first meeting and the subsequent meetings which we've held for HIV, for lung cancer and for narcolepsy, and we strive to keep improving along the way. We understand the effort and courage required for your contribution. On behalf of my colleagues, we really want to extend our sincere gratitude.

That's the first day, we have gratitude and appreciation for the second day too, but really it's a shout out for the participation on the first afternoon.

And now I'm going to switch gears and talk a little bit about the second day, April 26. The second day was more of a technical discussion, broadening the dialogue to include health care professionals, academics, researchers, pharmaceutical manufacture representatives and FDA staff. Its goal was to shine light on some prominent fundamental issues in drug development for CFS and ME, and gather information that is currently most valuable in helping FDA foster our role in the development.

Sandra Kweder: So this was - let me just kind of jump in here Sara - so the first day was really trying to capture the clinical status of what the condition is, you know, who are the people that have this condition, what is it they are experiencing. And so day two, which broadened the discussion to include people who may be in a position to help get drugs developed and help, think about how to study them. Is that a good way to put it?

Sara Eggers: Exactly - we had valuable contributions from researchers, clinicians, patients, industry representatives and our own colleagues. Key topics included drug innovation, drug re-purposing, regulatory pathways to facilitate drug development, considerations on endpoint development, endpoint development and qualification and current issues, challenges and opportunities when conducting clinical research.

Many of the points raised were really sharp and provocative, for example, the talk by Bernard Munos from InnoThink who spoke on drug development and drug discovery and the entire closing panel discussion on the path forward.

Like day one, we have received very positive feedback on the workshop from the speakers, the panelists, from participants and from the patient community. We plan to create a separate summary report capturing day two input, but given the current appropriations situation, we don't yet have the established target day for that. In a few minutes, my colleague Janet will describe other efforts directly building on this workshop.

Sandra Kweder: Hey - so should we go on to that, you know, one option will be take some questions now - if you have questions for Sara, rather than opening up the phone lines right now for that, write your questions down and we'll have an opportunity to - we'll - when we go to the open forum part of this conference call, you can then say this is a question for Sara to follow-up.

I'd like to step in now and introduce Dr. Teresa Michele, Terri Michele, who many of you know - she's been the FDA representative to the CFSAC and has been an active participant in all of our activities related to CFS and ME for a number of years now. So, and she is here with Dr. Janet Maynard, who is a medical officer in our center and I'm going to turn it over to Terri.

Teresa Michele: Very good, thank you Dr. Kweder, so first off, let me welcome everyone to the teleconference. Again, on behalf of the Division - so, I've had the privilege of serving on the CFSAC now since FDA made their decision back in January of 2011 to consolidate all of the chronic fatigue syndrome applications in the Division of Pulmonary, Allergy, and Rheumatology products, and the genesis of that was to provide one-stop shopping for sponsors coming in with chronic fatigue syndrome applications. And also, for us to try to have an impact on drug development in this arena, and so as a member of the CFSAC, I've really been privileged to get to meet many of you.

At this point in time, I am moving on to another position within the agency and I've been transitioning my role to Dr. Janet Maynard. So I'm very delighted to be able to introduce Dr. Maynard to you. Janet is a Rheumatologist in the Division of Pulmonary, Allergy and Rheumatology products. She's a clinical team leader and beginning with the November meeting, will be coming to the CFSAC meetings and serving as the ex officio member.

Janet has worked with me extensively over the last two years, and many of you will recognize her from her work on several different applications related to chronic fatigue syndrome. So she has - while she has perhaps not been in the limelight, she has been very much involved - and will be telling you about

her efforts along the lines of guidance and how she is spearheading that process for the FDA.

So at this point, I'll turn the mic over to Dr. Maynard and let her tell you about some of the other exciting things that FDA is doing in the arena of drug development.

Janet Maynard: Thank you so much Terri. So as Terri mentioned, my name is Janet Maynard and I'm an Acting Clinical Team Leader in the Division of Pulmonary, Allergy, and Rheumatology products at FDA. As Terri mentioned, my training is in internal medicine and rheumatology. And I just really want to emphasize that I'm very appreciative of the opportunity to work on issues related to CFS and ME as part of my activities at the FDA.

So first, I recognize that there are currently no therapies to treat CFS and ME and this represents a significant public health concern. There are four primary topics that I'm hoping to cover this afternoon in the context of current projects related to drug development to CFS and ME and the potential method to catalyze drug development.

These topics include recognition of a lack of approved therapies for CFS and ME, how FDA can assist with this issue, a description of drug development guidances and what is being done right now at FDA to help catalyze CFS and ME drug development. There will be an opportunity, as Dr. Kweder mentioned, for questions and discussions after I discuss the topics.

So first, FDA recognizes that there are currently no approved therapies indicated to treat CFS and ME. The lack of approved therapies indicated for the treatment of CFS and ME represents a public health concern. We are committed to finding avenues to collaborate with interested parties to foster

development for viable treatment options for serious diseases such as CFS and ME.

Second, FDA plays a role in drug development by working with pharmaceutical companies and other interested parties to assure clinical development programs meet their defined objectives. These objectives generally involve approval of a drug for the treatment of a disease. One tool that FDA uses to help pharmaceutical companies and other interested parties develop drugs is the guidance document.

The third topic I would like to cover is what is the guidance and how is it used. Guidance documents represent FDA's current thinking on a particular subject. These documents are intended to provide guidance to different individuals depending on the context of their use. In the context of drug development, the guidance is intended to assist the pharmaceutical industry in the development of drug products for treatment of a specific disease or type of diseases.

Guidance documents include information that will help pharmaceutical companies plan, design and perform clinical studies and perform data analysis. While guidance documents help the pharmaceutical industry develop products, they are not roadmaps. Rather, pharmaceutical companies are encouraged to discuss development plans with the FDA before starting studies to ensure that the clinical study design and analysis plan will meet defined objectives.

Drug development depends on many factors including whether the drug is being developed for the whole population of patients with the specific disease or a subset of patients. These factors are important to consider during the

drug development process and FDA will work with companies to individualize the process.

The fourth topic I would like to cover is what FDA is doing to catalyze CFS and ME drug development. Guidance documents represent one way that the FDA can help catalyze CFS and ME drug development. The FDA has recently published a draft guidance and is working on another guidance that will help catalyze drug development for CFS and ME.

The recently published draft guidance is for serious conditions such as CFS and ME. This draft guidance for industry involves expedited programs for serious conditions. The guidance outlines expedited programs available for qualifying products including fast track designation, break-through therapy designation, accelerated approval and priority review.

In addition, based on the results of the public workshop held on April 25 and 26, 2013, FDA is working on guidance for industry specifically for CFS and ME drugs. Although still in development with FDA, this document will provide advice for the pharmaceutical industry in order to expedite research on the development of medication to treat CFS and ME patients.

Importantly, as part of the guidance process there will be the opportunity for public comment and we would greatly appreciate the contributions of interested parties in those comments. Consistent with FDA guidance practices, a public notification will be announced in the Federal Register when the guidance has been released.

We encourage you to consider submitting comments to the public docket when it becomes available. When the guidance is initially released to the public, it will be in draft form. Regardless of whether it is draft or final, it will

provide important information for companies and investigators trying to develop drugs for CFS and ME.

In summary, FDA recognizes that there are no currently approved therapies indicated to treat CFS and ME. We are committed to finding avenues to collaborate with interested parties to foster development of viable treatment options for serious diseases such as CFS and ME. Currently, we are focusing our efforts on writing a guidance on drug development for CFS and ME as one method to catalyze drug development.

While guidance may catalyze drug development, a guidance is not necessary to allow drug development in CFS and ME. The FDA is extremely supportive of efforts to develop effective treatments for these debilitating conditions and is open to dialogue with the scientific, patient, and pharmaceutical communities. These discussions with companies and investigators are ongoing and are being encouraged.

So with that, I'd like to end my remarks and hand it back over to Dr. Kweder.

Sandra Kweder: Okay - alright, anything for folks - anything that Sara or Janet left out that you wanted to highlight? Alright - I want to open up for questions from everyone else on the phone who's not sitting here at FDA. I'd like to try and facilitate this a little bit, I'd like us to start with any questions that you might have for Sara Eggers surrounding the workshop and the posted summary of the workshop of day one. If you have questions for Sara, why don't you plan to, you know, indicate so by getting on line now and the operator will just kind of call on people in turn.

Coordinator: If you do have a question for Sara, please press star then one and to withdraw your question, press star than two. Stand by for your first question please - our first question comes from Billie Moore, your line is open.

Billie Moore: Thank you very much. We want to thank Dr. Mullin's group for doing such a good job with the Voice of the Patient Report, just another compliment to you for capturing so well what was so moving in that meeting. In spite of that, we were disappointed that the FDA had heard testimony for more than a decade at CFSAC and failed to act upon it. What I'm hearing today, particularly from Janet, is that you are acting upon it and this is very encouraging.

What we need now is exactly what you're describing plus possibly another stakeholders meeting to bring in the pharmaceutical companies who have already got drugs that are being used off-label by the leading doctors, the leading clinicians to treat the patients. However, the patients who are going to these doctors are very, very miniscule number compared to the number suffering, because they can't get to the doctors. We don't have a nationwide network of thousands and thousands of doctors who can treat this. We need to have a drug that is widely accepted by the medical community and that many doctors can use, not a few.

And therefore, the people who are already producing these drugs, they're anti-viral, Ampligen and Rituximab, and others these companies need to be brought to the table, you need to seek them out and the patient community will be more than happy to help you with that. And once again, thank you very much for this.

Sandra Kweder: Thank you for those comments. I will take them as comments and appreciate them. I didn't see them as questions.

Billie Moore: I did have one question.

Sandra Kweder: Yes.

Billie Moore: What is your timeline for the draft that Janet mentioned?

Sandra Kweder: Janet, you want to go ahead?

Janet Maynard: So, a guidance is usually a long process because we get input throughout the FDA, but we understand the importance of this document to hopefully catalyze drug development for CFS and ME, so our hope is to have draft guidance available for the public in the spring of 2014.

Billie Moore: Thank you very much.

Sandra Kweder. Thanks Billie. Okay, next question operator.

Coordinator: Our next question comes from Dr. Derek Enlander, your line is open.

Derek Enlander: Good afternoon, congratulations to Dr. Janet Maynard on her new position - I'm particularly interested in looking at Rituximab as previously mentioned. The work in Norway is creating quite a lot of interest, both in the side of the Atlantic and the other. How you will actually contact Janet to submit some ideas of plans to do this research? Could you tell me do we contact Dr. Maynard by letter or by email - or by both? Thanks and congratulations again.

Janet Maynard: Thank you, I really appreciate that. Just to make sure I understand your question, your question would be how to sort of work with the FDA about potentially bringing Rituximab to be developed as a drug for the treatment for CFS, correct?

Derek Enlander: Correct, how do we actually submit a proposal for looking at this drug under clinical conditions?

Janet Maynard: Well, there are guidelines available on FDA's website regarding how you would submit information and that sort - I don't know if we have our link right now on the CFS webpage that gives - with those other links and helpful information. That might be something--

Sandra Kweder: We can do that.

Janet Maynard: Yes, because really I want to say we really appreciate that as a suggestion because the process is called an IND and there are actually official guidances and official documents available through FDA website that outlines exactly the process - but I don't think we currently have the link on the CFS webpage to those other pages, but I'm looking at Randi and I think we can add that to the CFS webpage.

((Crosstalk))

Janet Maynard: Yes, there's a lot of information available, it's just kind of hard to see - exactly where it is and how to find it. It can be confusing, so we'll add that link to the CFS webpage and we really appreciate that suggestion, that's very helpful.

Sandra Kweder: Actually, I think there are two ways to think about it, one is if you and another group of investigators wanted to do this on your own, you could submit your own IND using marketed Rituximab, alternatively you could work through the company that manufactures the drug and get them to be the sponsor of the application and potentially even supply the drug.

And, you know, as always, these clinical investigations always come down to getting some funding and that, but those are two ways you can do it and some of the information that we have on the page will provide a link to - and we'll give you some tips about how to think of that.

Derek Enlander: What is the website page that one would actually go towards a fast track on Rituximab?

((Crosstalk))

Janet Maynard: Currently the FDA has a CFS webpage that has helpful information regarding CFS, so what I thought might be good is to add a link on that specific page to other information about how to submit an IND, just so it's easily accessible.

Randi Clark: This is Randi Clark, I can actually, as follow-up after this call, once I pull the links that Janet recommends, add them to the webpage. Then I'll send an email out to everyone involved in the April meeting and this meeting so that you have all the links together. They'll be under the main CFS webpage. If you're already familiar with that, we've been trying to keep it up to date. We recently made some changes to it to streamline it a bit. That way, you just have the email as a reminder if you're not as familiar with the webpage.

Janet Maynard: So, it sounds like you will receive the link and then hopefully it will get very clear and if there's any questions, of course, we're always willing to take any questions that come. So we really appreciate that idea.

Derek Enlander: Thank you.

Coordinator: And our next question comes from Jeannette Burmeister, your line is open.

Jeannette Burrmeister: Yes, hi - my question is for Dr. Maynard - I was wondering if you could give us an update in terms of what kind of draft applications are currently in front of the FDA for this disease. How many, what types of drugs and specifically, if you could let us know if it's true that there's an application for a combination drug currently pending which would be a combination of two already FDA approved drugs - FDA approved not for this disease but for other diseases, specifically anti-depressants and so the combination of a couple of anti-depressants - if that is something you're looking at right now. And you probably can't say, but I want to ask anyway, if you could let us know who the application is from?

Janet Maynard: That is a great question and I think you already realize that unfortunately there are limitations on the information that we can disclose. So we can not disclose when a sponsor comes to speak with us about developing products for any condition. The sponsors can disclose that information, but FDA, unfortunately is not at liberty to give the information about exactly which products are being developed or the exact number of products. So I think…

Jeannette Burmeister: Last year at the call, we were being told I believe it was nine drugs had applications pending and we were told they were all supplements in addition, well besides Ampligen, so you can't give us that information this year.

((Crosstalk)):

Terri Michele: This is Dr. Michele, I'm going to jump in here. That - where that information came from, that was a specific question that the CFSAC posed to FDA, was to ask us what were the number of applications for products in development for chronic fatigue syndrome and specifically for the number of INDs - exactly - so INDs are investigational new drug applications, that does not mean that the

products have gone through review and been ready for marketing or even that they've done clinical trials. It's just that somebody wanted to do a clinical trial in them.

Jeannette Burmeister: So are there any INDs currently?

Terri Michele: For this year?

Jeannette Burmeister: Is that something that's off the table right now?

Terri Michele: So, let me go there - so, we after much hoop jumping exercises got special permission to look at that information and we will request that permission again and perhaps Janet can give an update at the CFSAC meeting in November. We will not be able to tell you anything specific about the application, but we will try to give you a number.

Jeannette Burrmeister: If you could just give us the type of information you gave us last year, which was the number and, you know, it was basically only just supplements that would be very helpful or if it's not just supplements, you know, if you can't say what it is but that it is something other than supplements, I think people will find that very helpful and I appreciate your position right now. Thank you.

Coordinator: And our next questions comes from Gisela Morales-Barreto, your line is open.

Gisela Morales-Barreto: Hi, good afternoon, my name is Gisela Morales-and I'm calling as a caregiver and my question is probably touching on I was there in April and talking on the information I received there and thinking about all of this stuff and, you know, in the last few months and reading what you all, you know, submitted at the summary of the conference that, you know, it was wonderful.

The experience in person and reading the material has, you know, I think the first caller said you did capture a lot of what happens there, and it was amazing.

But I wanted to ask again, you know, one of the questions that I asked there when I was there, and my view of all of this, you know, as a caregiver and reading about this, is there, you know, definitely, you know, positions, you know, researchers working on this but then I get the feeling that the information, or what I foresee is that the information that everybody's working on, is not shared, you know, all the way through.

And I think that is, you know, number one a fact that affects the pharmaceutical companies also - to investigate this and create a product. Because everybody is working from a different angle if you know what I mean and how, and I don't know if it's the CDC or NIH or, you know, how can we get that information and it be shared in a way that attracts, again, the pharmaceutical companies to really look into this because you have repeated, you know, this afternoon and we know there is no product, no medications approved and there's a desperate need, you know, for that.

And I think of the silence and how do we bring the clients now to the information in a caring way that again, as a I said earlier, you know, attracts people to investigate this more, research it more and come up with something that is great probably not to everybody but at least the prospects, you know, to start - thank you.

Sandra Kweder: I'll take that - this is Dr. Kweder - I don't think that there's one answer to your question. I really appreciate your perspective that there seems to be a large number of people who are interested in this condition and particularly interested in developing treatments that would improve the lives of the

patients. Yet there doesn't seem to be a place where they can all kind of - where all that information can converge.

You know some of that comes through, you know, the traditional way this occurs and in other areas of medicine is publication of articles and the medical literature, that is a very, very powerful way of bringing, I would call for lack of a better term, mainstream attention to a disease and the challenges of developing therapies and so that's kind of a tried and true mechanism.

I think one of the challenges that we have in this field is that a lot of the folks who are spending time trying to do the research, they're also very busy clinicians and they don't have a lot of time to be writing up articles for it to be published in journals, it's just very - for anybody who's ever tried to do it, it's extremely time consuming.

And most people, you know, I think - investigators and researches have a little bit of an amnesia affect because when you're doing - you've promised yourself you'll never do this again and then you do it again because you have to but maybe you forgot how painful it was.

But that's one way, another is if there is a study group in a particular institution that tends to be able to attract investigators to share their experiences and develop a path forward. Another way is sometimes, and this is where we come in, Dr. Maynard talked about developing a guidance document, you know, the existence of a guidance document itself doesn’t mean that companies will all of a sudden, you know, take those helpful hints and go about the business of developing products to treat a particular disease.

But what it does do, is it does give them a sense of what the expectations are should they currently manufacture a drug that is being used off-label or that

someone has contemplated might actually be helpful with this disease. What companies always want to know is they want to know, what are the rules?

What do I have to do to get a drug developed - to test a drug and study it in this population? What is the general expectation? And we often see once a guidance document is published, a couple of months later after companies and investigators have had a chance to digest it a little bit, they start to come to FDA and go out to the community and have more conversations.

So all three of those ways, there's no one way that you bring people together but all three of those are ways to catalyze development of medical products and, you know, we're trying to pay attention to all three and we hope that, you know, through your efforts, you are as well. So thank you for that comment.

Gisela Morales-Barreto: Can I have a quick follow-up on what you said and I thank you for your answer but, you know, I'm always looking at the big picture Dr. Kweder, and one thing that surprises me every single day is that this, you know, illness has been around for a long, long time and the patient community is, you know, desperate as you can imagine and you saw it in April, the people who are paying it.

And I, you know, I live in Massachusetts and I see more and more cases every day of this and I see more and more because right now I'm surrounded by grief, you know, and I'm looking at this and I say what is going on here that the medical community is not really engaging into this process more to understand this illness, you know, better.

And I don't know if you have any advice or any comment, you know, to where the efforts for the patient community and the caregivers should be focusing more on right now, you know, to try to push this more quickly.

Sandra Kweder: My advice is to take it back to the medical community. I think that's one of the most important things that people who are taking care of patients with this who are frustrated can do, is take it to your medical community. Take it to the medical facilities who think about these things, who try to develop guidelines and generate that kind of enthusiasm because ultimately as well, anyone who wants to study the drug is going to have to go back to the medical community in order to help them do that.

It's really the energy has to come from a variety of places and the medical community is an important one and its people like yourself who are in the medical community who can do that better than anyone else.

Gisela Morales-Barreto: Thank you very much.

Coordinator: Our next question comes from Scott Shortenhaus your line is open.

Scott Shortenhaus: Thank you very much. I really appreciate all the work that the FDA is doing around this, it's very exciting. I am with industry with Eli Lilly and I just had a question, a policy related question, about how exactly the FDA is going to kind of put their findings into action in that very systematic way so that when, you know, reviewers are looking at this or the division is looking at this, it will - they'll be able to kind of understand, you know, what happened at the meeting, the survey that was accompanied with it and the report. I'm just wondering how will the division kind of implement the findings of this and how will that occur - thank you.

Sandra Kweder: I'll clarify for you - just for a second - thank you Scott. When you say the division, you mean the review division, DPARP - that's where Janet Maynard is from and Terri Michele came from. So your concern is how, you know, all

of this experience will ultimately reach those folks to take it all into account as they're thinking about drug development in this disease. Is that fair?

Scott Shortenhaus: Yes, you correctly captured it.

Sandra Kweder: Okay - so Janet, do you want to take that?

Janet Maynard: Yes, I don't think there's one or two things that can be taken out of a meeting - we're taking a lot of different information. I think some of the information has been highlighted in terms of ways that can help the pharmaceutical industry directly, including having a better sense of symptoms CFS and ME patients are suffering from.

So if you haven't read the report that Sara was discussing, I would really recommend that you look at that because I think it's an excellent way, as a pharmaceutical company that you can think about what clinical endpoints should be studied in a trial to really establish the efficacy of a drug.

The division is very open to having a pharmaceutical company address aspects of ME that are important to patients. So if you look at the report, those are clearly things that we would think would be important in a clinical trial. Does that sort of help answer how the workshop can be used?

Scott Shortenhaus: Yes, it does - I'm more on - I'm on the policy side and we're taking a look at how the FDA is implementing the benefit-risk framework across review divisions I guess, and so, specifically I was looking at appendix three of the report, I see where you've started to kind of fill out where you were hearing some of the different symptoms and things like that - I was just and not necessarily endpoints but also how you're going to take the findings and kind of - and put it into action with the reviewers themselves?

Sandra Kweder: We're in a little bit of a focus – at the meeting we were on the receiving end, so what we received there and is in the report is based on what we heard and then in the risk-benefit framework of how a drug review can be considered But that's to give you an idea of how we will be using this information based just on that one meeting. We're trying to think the meeting is extremely valuable at the beginning of our process that companies like yours might pursue and we have to know if these are things that you're going to be thinking of.

Scott Shortenhaus: Thank you very much, appreciate it.

Coordinator: Our next question comes from Tina Tidmore your line is open.

Tina Tidmore: Hi that is good timing, my question follows up on what Scott asked - first off I want to thank the FDA for having so many people joining in this meeting, I expected three and I have the disease so I'm not going to be able to remember all of your names but I appreciate there being so many people from the FDA involved in this meeting.

I wanted to say it has been said that this disease lacks measures or endpoints, however, besides the symptoms severity questionnaires, experts in the disease have discovered and the medical literature has shown that there are biological abnormalities in this disease including immune system, dysfunction, cortisol levels, blood pressure and many others and some of this goes back for 20 years. But it also includes what was discovered and now has been validated since 2007 and that is the two day CPET test and those drop and anaerobic thresholds as Christopher Snell discussed in the second day.

My question is will the guidance document that you're preparing include listing these biological abnormalities and/or symptoms of severity measures as endpoints or outcome measures that can be used in - by direct companies for this for this disease and will it include some that may not have been discussed at the April meeting - some others that are in the medical literature.

Janet Maynard: This is Janet Maynard and I'll try to answer that. So the purpose of the guidance document will be to sort of reflect how the division feels that efficacy might be demonstrated for a drug. So while this is still in process and in draft form, I guess that probably the guidance document will not go through all the background of CFS and ME or all biological abnormalities, but rather it will try to highlight these issues in the context of how it fosters and sort-of proves that a drug is effective for CFS and ME.

And we do plan to list some of the types of testing that you have referred to that have been used in both clinical practice and research. So things like exercise testing as ways of monitoring patients. So we'll try and touch on some of the issues that you have brought up.

I want to mention that the goal of the guidance isn't to sort-of tell sponsors every possible different thing that can be done to establish efficacy- but more to give a high level overview of the important aspects of the disease.

Sandra Kweder: In all of these guidances, what we tend to do is we try not to rule anything out unless, you know, there is something very specific we know about particular things not being useful in a particular disease. We know that you would never use an endpoint that really works for, I don't know, some kind, you know a completely unrelated illness necessarily and test it.

But we'd rather try to get examples of endpoint measures that we are aware of that have been shown to be helpful but leave the door open for conversations with investigators about others that they may think could be useful and to come in and talk to us about them and why they think they might be useful and how they want to show that.

Tina Tidmore: So basically the guidance document will have some but not all?

Sandra Kweder: Yes, we don't - it's almost impossible to have a full catalog of everything that's ever been used and it would take us forever to go through the literature to get that.

Tina Tidmore: Sure - okay, thank you.

Sandra Kweder: But we always tell companies is if you're going to use a particular endpoint or marker in a trial, you need to be able to scientifically justify why this is a good choice, you know, what do we know about that endpoint, how does it relate to the patient population you're studying and will it really tell you what you want to know - just basic scientific under pinnings.

Tina Tidmore: That is, an improved function.

Sandra Kweder: Yes.

Tina Tidmore: Okay - thank you.

Coordinator: And our next question comes from Courtney Miller, your line is open.

Courtney Miller: Thank you - good afternoon - I'm Robert Miller's wife and Robert has been a patient for more than 25 years and is unable to give these comments today so

he asked me to do it for him. He said, "I want to acknowledge and thank those at the FDA who work to put the drug development workshop together. The meeting was a very important start to fill the gaps in treatment for suffering patients everywhere. But it is only as good as the follow-up going forward and the speed of bringing treatments to patients.

I believe pharmaceutical companies need to see a commitment from the FDA to approve safe and effective products and they need clear, clinical endpoints to measure drug benefits or they won't come to the table, and they haven't. FDA has the power to bring together the expert clinicians to agree on those endpoints. And that's what I'm asking you to do.

You are drafting guidance which I'm glad to hear, and I would ask if you are, or if you will, consult the clinicians who best understand the seriousness and treatability of this illness. The same six clinical experts have participated in studies across the federal agencies and Dr. Lipkin’s XMRV study at NIH to the CDC's clinical assessment study and the private studies which have produced astounding results of immune activation and bio-markers just recently disclosed on a CFS patient.

The experts are there, they have vast experience treating and measuring progress and relapse and I urge you to convene them to come to consensus on end points that can be included in your guidance and that can bring CFS into the twenty-first century with approved medical treatments like MS.

We know the FDA can take initiative in creating special processes, they're doing it for Alzheimer's; we are thrilled that you are doing it, we just ask that you bring in the experts to outline what the clinical endpoints that pharmaceutical companies can start off with. Thank you."

Sandra Kweder: Well Courtney, thank you for sharing those comments, one of the things that we do is when - is we try and take - we try to get input from a broad variety of sources. We did some of that and I think we heard a great deal of this at the workshop last April as well as our own experience in the drugs that we've looked at as well as the medical literature, much of which has been published by, you know, obviously by experts in the field.

And we usually - what we'll do is we'll put together a draft guidance document to talk about some of that and we'll put it out for public comment and convene some of those experts once we have the whole thing pulled together to try and refine it. Because the endpoints for one aspect of the condition may not be the right endpoint for a different aspect of the condition.

And different aspects of the condition might be studied depending on the agent that's being investigated. And so what's appropriate to use as an endpoint in drug class A is not the same as drug class B. So those are all really good comments and we expect that we'll continue to seek input. So thank you very much.

Coordinator: And our next participant is Lori Kroger, your line is open.

Lori Kroger: Hello, thank you for this opportunity. I want to first congratulate Dr. Maynard for her new position and thank you to the FDA and Dr. Mullin for capturing the severely ill in the patient's voice report. I am President/CEO and also a patient of Pandora Org and we are the largest patient organization and because of that I receive many phone calls from suicidal patients, in fact, I got a call yesterday from a patient that was wanting to end her life.

I listen, I cry and I try to offer them hope. The most popular reason or the most important aspect of suicide is patients are extremely sick and they feel

like they don't have future because there are no treatments and getting therapy and they feel like they're rotting in bed. They want access to treatment like Virovir, Ampligen, Rituximab, anti-virals and they would like insurance coverage so they can afford those also.

They also, as we have heard from a couple of other commenters, is that they want a second stakeholder meeting with drug companies and experts. I would like to offer a nugget of hope to these patients when I get a call and I'm sure you do too. So can you tell me when a second stake holder meeting for MECFS will take place with industry and experts?

Sandra Kweder: The answer to that is - we don't have a date to provide you with. I think one of the challenges is figuring out how - what drug companies we would want to invite. And, you know, that is something to contemplate and I also think that's something the patient organizations, that's something that could be hosted even without government engagement, some sort of a workshop or a committee of experts of drug companies with the experts and the patients who use them - they are important to engage. We do not have a specific plan for such a stakeholder meeting at this point in time. I can't promise you a date, I know we do have a list here of - here at the FDA site for this call and I know that there are people from industry who are on the call and I'd like to know from them if you have suggestions for what would be helpful from your standpoint because obviously you are on the call for a reason and I won't call out your name, I won't embarrass you to that degree but I know there are at least five of you.

Lori Kroger: I would like to hear from them too. During the April meeting there was a chart that showed symptoms, testing for the symptoms and compiled the markers and what drugs could be used off-label and what patients are using off label.

Is that included in your guidance document for measures? Because I think that would be most helpful to drug companies.

Janet Maynard: Thank you for that suggestion, I will go back and look at that. We're not currently planning on including that chart in the guidance document, but we do point pharmaceutical companies to go look at the report that was published because we do think that there is a wealth of important information in that document that really compliments what we were planning on including in the guidance document. So we're thinking of either trying a complimentary document but they might not have the same information.

Lori Kroger: Okay - that is a great document and if any of the drug people that are listening from drug companies would like that, Pandora Org.net has that document and we would be very happy to provide you with that to help you in your development in medications for us. Thank you.

Sandra Kweder: Thank you for your comments - very helpful.

Coordinator: And our next question comes from Dr. Faith Newton, your line is open.

Faith Newton: Yes, good afternoon - I do educational research with Delaware State University and also a parent of a 17 year old who has had CFS since fifth grade. I would like to know, what is the path forward for plans for developing treatments for pediatric ME/CFS?

Janet Maynard: In terms of a guidance document, our guidance document wasn't planning on sort of specifically talking about pediatric, but the guidance document does say that we are encouraging development for all different subjects, whether that be certain symptoms of CFS and ME or specific age groups. So we're

really trying to make this guidance as encouraging as possible in terms of saying the broad range of patients who are affected by this.

Terri Michele: Yes, this is Dr. Michele - just to add to what Dr. Maynard said, being that CFS is no longer an orphan disease, it now falls under PREA, which is Pediatric Research Equity Act and as such, if a product were to be approved for chronic fatigue syndrome, the sponsor would be obligated to consider development in the pediatrics as well and would have to have specific pediatric plan during their development process that was vetted through the agency.

Faith Newton: Thank you very much.

Sandra Kweder: And to add to that, that doesn't mean that development for pediatric aspect of the condition need to wait until after adult development is done. We have many examples of where pediatric development occurs in parallel.

Faith Newton: Thank you, I appreciate the time.

Coordinator: And our next question will come from Jennifer Spotila, your line is open.

Jennifer Spotila: Hi everyone and thank you for today's call. I also want to thank Dr. Michele for her service on the CFSAC and I hope we can expect the same kind of participation from Dr. Maynard and we look forward to welcoming you in November.

I have a couple of questions and a comment, first I was wondering if any progress has been made in patient-reported outcome or bio-marker qualification. I understand that is a separate process that FDA makes available - I'm wondering if anything has happened since the April meeting to advance that and then the second piece is a comment coming from the training I had as

a member of the patient representative program at FDA - a number of the representatives from all different diseases really put a challenge forward to FDA at that meeting asking that you find more and creative ways to integrate patients earlier in the process, far before a drug comes before an advisory committee.

And I know that the PFDD initiative is a part of that, but I'm wondering what role our patient community can play in the development of the guidance document, even before the draft is published in the spring.

I think that incorporating the patient viewpoint earlier will only produce a better document in the end, thank you.

Janet Maynard: That's a two part question - the first part was whether we were aware of any advancement that have been made in regard to patient reported outcome? Is that correct?

Jennifer Spotila: In PROs and bio-marker qualification.

Janet Maynard: And I'm not aware of any new developments after that meeting related to the patient report outcomes or bio-marker qualifications in relations to CFS and ME. With that being said, again, the guidance document plans on being as inviting and comparable in terms of those issues and sort of recognizing while there may not be that the patient reported outcome or bio-markers have been qualified at this point for CFS and ME, that we are willing to work with pharmaceutical companies to help with that process because we understand the process.

The second issue you brought up is, you know, that at the meeting it was stressed that we should have more creative ways to include patients in the

drug development process, generally, and also specifically in terms of spreading the guidance side of this - correct?

Jennifer Spotila: Correct.

Janet Maynard: So I totally agree with you and I think that the input that we've had, has been really helpful and in my mind, we're thinking about how we can improve things in a guidance document or change the website so that we have to make sure that we're being as helpful as possible in the drug development process.

So we are very appreciative of your involvement in this call today and all of the input that we've gotten from interested parties regarding this issue. And we'll continue to think of other ways, but I would encourage you to sort of also participate when the draft guidance is available to give comments at the public docket.

Sandra Kweder: Yes, and I want to support Janet in that - a lot of the input that we got from the workshop itself will go directly into the guidance document as well as some of the things we hear in these conversations through conference calls. We are restricted, there are rules about, not of our writing, about what - how we can go about a process of writing guidance documents, you know, so for example, if somebody asks us when we would expect it to be published, we're not even supposed to speculate on what that time is. It's just kind of one of those roles that the government makes us follow.

So we can't - it's hard for us to directly incorporate patients in the writing of such a document. But we feel like we have a lot we can incorporate from what we've already gathered so far and we will seek your input once it's published in different ways to get to make it even better so that when it's final form, its better.

Coordinator: And our next question comes from Donna Pearson, your line is open.

Donna Pearson: Hi - thank you very much, I appreciate the opportunity. My question actually has two parts. The first part is if you could please explain a little bit better for the patients who are listening what exactly expedited programs mean when you say priority review, fast track acceleration, are we talking about two years, ten years - twenty years?

And secondly, how can we be sure that you will have experienced and informed people that are serving as advisory panels when you're reviewing drugs? We were at the Ampligen advisory committee meeting and it appeared to us that a number of those people really did not understand the disease and therefore it was difficult for them to truly weigh the risk and the benefits. So how can they be better informed as well?

Sandra Kweder: Okay - Janet you want to take one of those?

Janet Maynard: Sure - I think the first question was to define what exactly is reviewed in the expedited program for serious conditions? I agree the terminology is confusing to not only us but the industry and that is one of the reasons there is guidance available for these topics because it's sort of confusing in how to apply the different things.

So I would encourage you, if you Google the term you will find the guidance on that issue and we have a really helpful table that sort of goes over what the different programs are and which state of the development you would refer to and I think Randi said she can add that link to the CFS webpage. I hope is helpful to you.

So I think really in terms of your question, sort of when will there be a drug available, I think what you're getting to is for CFS and ME. I can't give you a number. But I think if you have a chance to look at the guidance it will be helpful..

Terri Michele: This is Terri Michele - those comments on the second part of your question, which is the advisory panel members and how do we chose and how do we make sure that we have the best expertise on all of our committees. So the advisory panels are made up of two different groups.

The first group is a standing panel and there are actually 34 different advisory panels at the FDA covering a variety of different areas. Chronic fatigue syndrome drugs go to the rheumatology advisory panel and there's a standing committee made up of a statistician as well as clinical research experts in the area of rheumatology.

So because everything goes to that panel regardless of what the specific disease area within rheumatology is, we make sure that the standing committees have a variety of different experts on them. Some may be experts on gout; some may be experts on lupus and cover a variety of different areas.

But all of them have a very high level of expertise in clinical trials and bring something unique to the table. In addition to that, we supplement our committees with experts in chronic fatigue syndrome, if that's what we're talking about. And specifically bring on several members of the panel who have particular expertise in the area that we're discussing on that particular day and so the purpose of this is to give FDA a wide variety of opinions and the variety adds richness to the conversation.

So that's kind of where the thinking goes and why not every single person on a panel has the same level of expertise, because these are very complex applications and as such, you need to bring together a whole of different opinions and a whole lot of different expertise to the table to begin to think about things. Dr. Kweder, did you have anything to add to that?

Sandra Kweder: I think it's a good summary Terri, in order to, you know, one of the challenges that we often has is and it's not unique to this condition, but just as a general comment, we often have the challenge of some of the experts who we would like to have sit on the panel, we can't have sit on the panel because they are considered to have a conflict of interest.

So for example, we often find ourselves where we can't get an expert in a particular disease because that expert, him or herself has been deeply involved in clinical studies of the disease. And because of that, they are considered by the rules governing advisory panels in general, to have a conflict of interest.

And so they are excluded from the conversation, it's very, very frustrating for us and we work very hard to find good experts and sometimes where we know of people we don't even go through the exercise of inviting them because we already know what their conflicts are and that they would never pass.

And so it's a continuing challenge and we are often in a position of reaching out to communities to ask for suggestions for additional experts.

Donna Pearson: So I would just ask for future panels are given all of the information that you've gathered at the meeting in April because I remember at least one and maybe more than one government employee commenting that they really didn't truly understand the disease until that day, until they had heard, so I

think that was obviously very valuable information that was shared that day and I would hope that you would share it with future panel members.

Sandra Kweder: That's a great suggestion, that's a really great suggestion, thank you.

Donna Pearson: Thank you.

Coordinator: Our next question comes from Matina Nicholson, your line is open.

Matina Nicholson: Hello?

Sandra Kweder: Hello.

Matina Nicholson: Can you hear me?

Sandra Kweder: Yes.

Maina Nicholson: Okay - my question is two-fold, lumping ME and CFS together in the document provided, we separate the two diseases out because if we lump them together I don't think we're going to get the effect that we need so because ME is not CFS and second how does the IOM contract - how does that affect policy because there's a lot of people against it and the experts come to an agreement. Those are my questions.

Janet Maynard: Maybe I can address the first part of your question which was about whether we are lumping CFS and ME together and I think that's sort-of a really interesting point that we've also summarized in the voice of a patient from the workshop. So, currently FDA is using the term CFS, ME and CFS and ME interchangeably in describing these conditions and at this time the FDA does

not endorse any particular definition. We're hoping that drug developers will focus on the measures of benefit in a defined patient population.

We're sort of leaving it up to pharmaceutical companies to define which patient population they would like to study and establish that. Does that answer the first part of your question?

Maina Nicholson: Yes. If you lump them together, it's just concerning as a patient trying to get a drug here fast.

Sandra Kweder: Can you ask the second part of your question again?

Maina Nicholson: My second question is about the IOM contract and case definition for research and notice of the disease and they are going to - they're set to do that. There's a group of patients against that and how's that going to impede on the definition used for research.

Sandra Kweder: Just a general comment, I would say that from our standpoint, anytime a large organization with the status of something like the Institute of Medicine agrees to further study and try and help articulate information about a medical condition, it's a good thing. In general, it's a good thing, so we don't see this, you know, whatever the IOM has dealt with, we see as hopefully enriching the discussion and providing additional ways for people to think about these conditions and find ways to develop medical products.

And equally as important is to help find ways to bring the conversation about the importance of these conditions into clinical - into the clinical medicine communities as one of our previous questions pointed out. We think that's really important, it's one of the ways that you really - we will all succeed in getting drugs to treat patients.

When you have, you know, discord among, you know, primary care physicians who aren't necessarily experts but framing the disease in a way that they can grasp onto it, recognize it and help encourage companies and people who are in the research community to really fund and develop studies and therapies to treat it.

So in general, we see it as a good thing, we do understand that there are people who aren't happy with it, it does appear that it's moving forward and I think the most important thing from our perspective to do is to try and be part of the conversation whenever we can and try to ensure that the community is engaged with the IOM in a constructive way. And that in the end, that good will come of it.

Matina Nicholson: Thank you and thank you so much for the workshop invitation.

Sandra Kweder: And I'd just like to add one thing to that, one of the reasons that these discussions in the general medical community that I think the IOM can facilitate around and be important is, you know, none of the companies on the call took my challenge to speak up, but I know that one of the things companies always worry about is, you know, if I build it will they come? And in their minds it's not just will people treat patients with my medicine but will insurers pay for the medicine?

And so the definition that will speak to payers that yes, this is an important medical condition and you should reimburse for the therapies to treat this condition. Some of that's the kind of thing that can come out of these kinds of reports that the IOM develops. Terri, do you have any comments about that?

Theresa Michele: I think that you outlined that beautifully because one of the concerns that I've heard from companies is that they may have difficulty getting reimbursement for approved products because the definitions are so wishy-washy that insurers may not be willing to pay for a product.

So I think anything that we can do to facilitate definitions and importantly, to facilitate widespread uptake of these definitions by the medical community and a group with the status of the Institute of Medicine putting their shoulder to wheel on this, I think really does help augment those efforts of the patient community.

Sandra Kweder: I think we have time for maybe one more question.

Coordinator: And our last question will come from Rifka Sullen, your line is open.

Rivka Solomon: Hi, can you hear me?

Sandra Kweder: Yes.

Rivka Solomon: Okay - thank you, first of all thank you for this meeting, I appreciate everybody including the patients who are here, I know it can take a great deal of energy and effort to be here. I just wanted to reiterate what Lori talked about earlier that we did submit this table of potential meds to repurpose. It was a patient driven effort and the table has over 100 meds already in use by patients and their doctors. So these meds can certainly be used for repurposing and thus the companies that make these meds will be good companies to invite to any subsequent meetings where pharmaceuticals are invited.

So that table I think will be key, it took months of our efforts to put that table together and so I would encourage you to use that and Lori and I will talk and

make sure you have the most updated version of that. Somebody did mention on the FDA side of this call that it will be great if patients could organize such a meeting and I just wanted to make sure that the FDA understands why something like that would be extraordinary difficult for the patient.

We are very, very sick and many of us are so sick that we're bedridden and homebound and so organizing something like that would be extraordinarily difficult and many of us do not have what, for example, autism, the autism community has like these warrior moms who are fighting so hard for their kids or the AIDS community activists had a community like the LGBT community to fall back on.

In our situation, because of the name chronic fatigue syndrome, many of our families never believed the severity of our illness and they sort of just think, well, why don't we exercise our way out of it. So we don't have the families behind us to help organize these types of conferences and the patients are very sick. So that's the reality of our situation, meanwhile we would love it if the FDA were able or were in a position to organize a meeting where we were invited and I think that table would be a great starting point.

Sandra Kweder: Thank you very much, your comments are greatly appreciated. I think we have - I'd like to close our call now and I can't believe it's been an hour and a half, I want to thank you all for your participation and I would like to open it up to see if anyone here are the table or on the phone has any final comments based on what you've heard from the callers today. Sara—anything from you?

Sara Eggers: No, I would only want to reiterate my thanks for your input today and the input we've gotten all throughout this process.

Sandra Kweder: Theresa, do you have any anything?

Theresa Mullin: Thank you for all the input.

Sandra Kweder: Janet?

Janet Maynard: Thank you - I appreciate everyone's kind words today and I look forward to working together.

Sandra Kweder: And I will just close and thank everyone as well and assure you that we - our doors are open, we are open for business and we are continuing to press forward to try and improve the situation of all of you on this call who suffer from this condition or your family member or your patient. So thank you very much for spending this time with us today.

Coordinator: And that does conclude today's conference, thank you for your participation, you may disconnect your line at this time.

END